What is claimed is:

1. An isolated polypeptide comprising a JAM domain consisting essentially of an amino acid sequence of HXHXXXXXXXXXXD (SEQ ID NO. 1), wherein H is histidine, D is aspartate, and X is any amino acid and wherein the JAM domain is not adjacent to an amino acid sequence that is naturally adjacent to the domain.

2. The polypeptide of claim 1, wherein the JAM domain provides peptidase activity.

3. The polypeptide of claim 1, wherein the JAM domain provides isopeptidase activity.

4. The polypeptide of claim 1, wherein the JAM domain is a metalloenzyme active site.

5. The polypeptide of claim 1, wherein the JAM domain consists essentially of an amino acid sequence of GW(Y/I)H(S/T)HPXXXXXXSXXD (SEQ ID NO. 2), wherein G is glycine, W is tryptophan, Y is tyrosine, I is isoleucine, H is histidine, S is serine, T is threonine, P is proline, D is aspartate, X is any amino acid, Y/I is either Y or I, and S/T is either S or T.

6. An isolated crystalline polypeptide, wherein the polypeptide comprising a JAM domain consisting essentially of an amino acid sequence of HXHXXXXXXXXXXD, wherein H is histidine, D is aspartate, and X is any amino acid.

7. The crystalline polypeptide of claim 6, wherein the JAM domain provides peptidase activity.

8. The crystalline polypeptide of claim 6, wherein the JAM domain provides isopeptidase activity.

9. The crystalline polypeptide of claim 6, wherein the JAM domain is a metalloenzyme active site.

10. The crystalline polypeptide of claim 6, wherein the polypeptide is COP9/signalsome, 26S proteasome, AMSH, AMSH1, or AMSH2.

11. The crystalline polypeptide of claim 6, wherein the JAM domain consisting essentially of an amino acid sequence of GW(Y/I)H(S/T)HPXXXXXXSXXD (SEQ ID NO. 2), wherein G is glycine, W is tryptophan, Y is tyrosine, I is isoleucine, H is histidine, S is serine, T is threonine, P is proline, D is aspartate, X is any amino acid, Y/I is either Y or I, and S/T is either S or T.

12. An isolated monoclonal antibody that specifically binds to an epitope within a JAM domain of a polypeptide, wherein the JAM domain consists essentially of an amino acid sequence of HXHXXXXXXXXXXD, wherein H is histidine, D is aspartate, and X is any amino acid.

13. The monoclonal antibody of claim 12, wherein the polypeptide is COP9/signalsome, 26S proteasome, AMSH, AMSH1, or AMSH2.

14. The monoclonal antibody of claim 12, wherein the JAM domain consists essentially of an amino acid sequence of GW(Y/I)H(S/T)HPXXXXXXSXXD (SEQ ID NO. 2), wherein G is glycine, W is tryptophan, Y is tyrosine, I is isoleucine, H is histidine, S is serine, T is threonine, P is proline, D is aspartate, X is any amino acid, Y/I is either Y or I, and S/T is either S or T.

15. A method of identifying an inhibitor of a polypeptide by rational drug design wherein the polypeptide comprises a JAM domain consisting essentially of an amino acid sequence of HXHXXXXXXXXXXD, wherein H is histidine, D is aspartate, and X is any amino acid, the method comprising

designing a potential inhibitor for the polypeptide that will form a bond with the JAM domain based upon the crystal structure co-ordinates of the polypeptide,

synthesizing the inhibitor, and

determining whether the potential inhibitor inhibits the activity of the polypeptide.

16. The method of claim 15, wherein the polypeptide is COP9/signalsome, 26S proteasome, AMSH, AMSH1, or AMSH2.

17. The method of claim 15 wherein the potential inhibitor will form a bond with a metal ion bound by the JAM domain.

18. The method of claim 15, wherein the peptidase activity of the polypeptide is de-neddylation.

19. The method of claim 15, wherein the peptidase activity of the polypeptide is de-ubiquitination.

20. The method of claim 15, wherein the JAM domain consists essentially of an amino acid sequence of GW(Y/I)H(S/T)HPXXXXXXSXXD (SEQ ID NO. 2), wherein G is glycine, W is tryptophan, Y is tyrosine, I is isoleucine, H is histidine, S is serine, T is threonine, P is proline, D is aspartate, X is any amino acid, Y/I is either Y or I, and S/T is either S or T.

21. A method of deconjugating a modifier protein from a target protein, wherein the modifier protein is conjugated to the target protein via a peptide bond between the carboxy terminus of the modifier protein and a free amino group of the target protein comprising contacting the target protein to a polypeptide comprising a JAM domain consisting essentially of an amino acid sequence of HXHXXXXXXXXXXD, wherein H is histidine, D is aspartate, and X is any amino acid.

22. The method of claim 21, wherein the JAM domain consists essentially of an amino acid sequence of GW(Y/I)H(S/T)HPXXXXXXSXXD (SEQ ID NO. 2), wherein G is glycine, W is tryptophan, Y is tyrosine, I is isoleucine, H is histidine, S is serine, T is threonine, P is proline, D is aspartate, X is any amino acid, Y/I is either Y or I, and S/T is either S or T.

23. The method of claim 21, wherein the target protein is a cullin protein.

24. The method of claim 23, wherein the target protein is Cul1, Cul2, Cul3, Cul4A, Cul4B, or Cul5.

25. The method of claim 21, wherein the target protein has ubiquitin ligase activity.

26. The method of claim 21, wherein the target protein is part of a protein complex having ubiquitin ligase activity.

27. The method of claim 21, wherein the modifier protein is NEDD8, UBL1, SMT3H2, SMT3H1, APG12, FAT10, Fau, UCRP, URM1, or UBL5.

28. The method of claim 21, wherein the polypeptide is a polypeptide complex of COP9/signalsome.

29. The method of claim 21, wherein the polypeptide is AMSH, AMSH1, or AMSH2.

30. The method of claim 21, wherein the target protein is exposed to the polypeptide *in vitro*.

31. The method of claim 21, wherein the target protein is exposed to the polypeptide *in vivo*.

32. A method of screening for an agent that affects deconjugation of a modifier protein from a target protein, wherein the modifier protein is conjugated to the target protein via a peptide bond between the carboxy terminus of the modifier protein and a free amino group of the target protein, the method comprising

incubating in the presence and absence of a test agent, the target protein and a polypeptide comprising a JAM domain consisting essentially of an amino acid sequence of HXHXXXXXXXXXD, wherein H is histidine, D is aspartate, and X is any amino acid,

determining the effect of the test agent, wherein an increase or decrease in the amount of the target protein not conjugated to the modifier protein caused by the test agent is indicative of an agent affecting deconjugation of the modifier protein from the target protein.

33. The method of claim 32, wherein the JAM domain consists essentially of an amino acid sequence of GW(Y/I)H(S/T)HPXXXXXXSXXD (SEQ ID NO. 2), wherein G is glycine, W is tryptophan, Y is tyrosine, I is isoleucine, H is histidine, S is serine, T is threonine, P is proline, D is aspartate, X is any amino acid, Y/I is either Y or I, and S/T is either S or T.

34. The method of claim 32, wherein the target protein is a cullin protein

35. The method of claim 34, wherein the target protein is Cul1, Cul2, Cul3, Cul4A, Cul4B, or Cul5.

36. The method of claim 32, wherein the target protein has ubiquitin ligase activity.

37. The method of claim 32, wherein the target protein is part of a protein complex having ubiquitin ligase activity.

38. The method of claim 32, wherein the modifier protein is NEDD8, UBL1, SMT3H2, SMT3H1, APG12, FAT10, Fau, UCRP, URM1, or UBL5.

39. The method of claim 32, wherein the polypeptide is a polypeptide complex of COP9/signalsome.

40. The method of claim 32, wherein the polypeptide is AMSH, AMSH1, or AMSH2.

41. The method of claim 32, wherein a test agent decreasing the amount of the target protein not conjugated to the modifier protein is indicative of an agent decreasing deconjugation of the modifier protein from the target protein.

42. The method of claim 32, wherein the target protein has the activity of peroxidase, alkaline phosphatase, or luciferase.

43. The method of claim 32, wherein the target protein is a fluorescent protein.

44. The method of claim 43, wherein the fluorescent protein is selected from the group consisting of green fluorescent protein, yellow fluorescent protein, cyan fluorescent protein and dsRed.

45. The method of claim 43, wherein the target protein is a fluorescent protein via chemical modification.

46. The method of claim 32, wherein the target protein causes production of a detectable signal upon deconjugation from the modifier protein.

47. The method of claim 32, wherein the polypeptide is a polypeptide complex of 26S proteasome.

48. The method of claim 32, wherein the polypeptide is a polypeptide complex of 26S proteasome and the modifier protein is an ubiquitin.

49. The method of claim 47, wherein the incubation is conducted in the presence and absence of the test agent, the target protein, the 26S proteasome, and a 20S inhibitor.

50. The method of claim 47, wherein the incubation is conducted in the presence and absence of the test agent, the target protein, the 26S proteasome, a 20S inhibitor, and ATP.

51. The method of claim 50, wherein the incubation further includes an inhibitor of deubiquitination by an ubiquitin isopeptidase.

52. The method of claim 47, wherein the target protein not conjugated to the modifier protein is not degraded.

53. The method of claim 47, wherein the target protein is Sic1.

54. The method of claim 47, wherein the 26S proteasome is purified from *S. cerevisiae*.

55. The method of claim 47, wherein the 26S proteasome is purified from eukaryotic cells.

56. The method of claim 47, wherein the 26S proteasome is purified from human cells.

57. The method of claim 32, wherein the test agent is a member of a compound library selected from the group consisting of hydroxamate compound library, reverse hydroxamate compound library, carboxylate compound library, thiol compound library, and phosphonate compound library.

58. An agent identified by the method of claim 15.

59. An agent identified by the method of claim 32.

60. An agent identified by the method of claim 41.

61. A method of increasing conjugation of a modifier protein to a target protein, wherein the modifier protein is conjugated to the target protein via a peptide bond between the carboxy terminus of the modifier protein and a free amino group of the target protein in a cell comprising inhibiting the activity of a polypeptide comprising a JAM domain consisting essentially of an amino acid sequence of HXHXXXXXXXXXXD, wherein H is histidine, D is aspartate, and X is any amino acid, thereby increasing the conjugation of the modifier protein to the target protein.

62. The method of claim 61, wherein the JAM domain consists essentially of an amino acid sequence of GW(Y/I)H(S/T)HPXXXXXXSXXD (SEQ ID NO. 2), wherein G is glycine, W is tryptophan, Y is tyrosine, I is isoleucine, H is histidine, S is serine, T is threonine, P is proline, D is aspartate, X is any amino acid, Y/I is either Y or I, and S/T is either S or T.

63. The method of claim 61, wherein the polypeptide is COP9/signalsome.

64. The method of claim 61, wherein the polypeptide is AMSH, AMSH1, or AMSH2.

65. The method of claim 61, wherein the polypeptide is 26S proteasome.

66. The method of claim 61, wherein the target protein is a cullin protein.

67. The method of claim 66, wherein the target protein is Cul1, Cul2, Cul3, Cul4A, Cul4B, or Cul5.

68. The method of claim 61, wherein the target protein has ubiquitin ligase activity.

69. The method of claim 61, wherein the target protein is part of a protein complex having ubiquitin ligase activity.

70. The method of claim 61, wherein the modifier protein is NEDD8, UBL1, SMT3H2, SMT3H1, APG12, FAT10, Fau, UCRP, URM1, or UBL5.

71. A method of treating a condition, wherein the condition is neoplastic growth, angiogenesis, infection, chronic inflammation, asthma, ischemia and reperfusion injury, multiple sclerosis, rheumatoid arthritis, or psoriasis comprising administering an agent identified by the method of claim 41 to a subject in need of such treatment.